

Stereological and Histopathological Evaluation of the Effects of Indole-3-Carbinol on the Heart-Brain Axis via the Ventromedial Hypothalamus in an Obesity Model

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Abstract

Objective: This study aimed to investigate the effects of indole-3-carbinol (I3C) on the heart and ventromedial hypothalamus (VMH) in an experimental obesity model using histopathological and stereological methods, and to evaluate its potential contribution to the heart-brain axis in the context of energy homeostasis.

Materials and Methods: A total of 24 male Wistar rats were divided into three groups: control, obese (high-fat diet), and obese + I3C. Obesity was induced by a high-fat diet over a period of 12 weeks. I3C treatment was administered during the last 4 weeks. At the end of the experiment, heart and brain tissues were fixed in 10% neutral buffered formalin, processed routinely, and embedded in paraffin. Sections (4–5 µm thick) were stained with Hematoxylin-Eosin (H&E). In heart tissue, cardiomyocyte diameter, cellular hypertrophy, interstitial edema, vascular congestion, inflammatory cell infiltration, and possible fibrotic changes were evaluated semi-quantitatively. Cardiomyocyte size and volume were also estimated using stereological methods. In VMH sections, neuronal density, cellular organization, neuronal morphology (nuclear clarity and cytoplasmic integrity), glial cell proliferation, and neurodegenerative findings were assessed. Neuron number and volumetric changes were analyzed stereologically using the unbiased fractionator and Cavalieri methods.

Results: In the obese group, heart tissue showed cardiomyocyte hypertrophy, increased cell diameter, interstitial edema, vascular congestion, and focal inflammatory cell infiltration. Disruption of myocardial architecture and early signs of fibrotic remodeling were observed. In the VMH, a decrease in neuronal number, disorganization of neuronal arrangement, pyknotic nuclei, and cytoplasmic degeneration were detected. Increased glial cell presence (reactive gliosis) and disruption of neuropil integrity were also observed. These histopathological alterations are considered to negatively affect VMH functions related to energy balance and appetite regulation. In the obese + I3C group, a reduction in cardiomyocyte hypertrophy, decreased edema and vascular congestion, and partial restoration of myocardial architecture were observed. Inflammatory infiltration was reduced, and fibrotic changes were less pronounced. In the VMH, increased neuronal number, improved neuronal morphology, restoration of nuclear and cytoplasmic integrity, and reduced glial activation were noted. Neuropil organization and overall cellular architecture were markedly improved.

Conclusion: Indole-3-carbinol ameliorates obesity-induced cardiac structural alterations and neurodegenerative changes in the ventromedial hypothalamus at the histopathological level. These findings suggest that I3C may support energy homeostasis through modulation of the heart-brain axis.